REMARKS/ARGUMENTS

The Pending Claims

Claims 1 and 7-10, 12, and 16-22 are pending and are directed to a method for inducing an immunological response against a malignant pancreatic cell in an individual.

Amendments to the Claims

The claims have been amended to point out more particularly and claim more distinctly the invention.

In particular, claim 1 has been amended to remove the extraneous "a" from part (c) and to replace "modified" with "wobbled." Claim 12 has been amended to recite the feature of claim 13 (now canceled). In view of the cancelation of claim 13, claim 16 has been amended to depend from claim 12.

No new matter has been added by way of these amendments to the claims.

Summary of the Office Action

The Office objects to claim 1.

The Office rejects claims 1, 7-10, 12, 13, and 16-22 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite.

The Office rejects 1, 7-10, 12, 13, and 16-22 under 35 U.S.C. § 103(a) as allegedly obvious in view of Laidlaw et al. (U.S. Patent 7,273,605), Pecher (WO 01/24832), and Kotera et al. (*Cancer Res., 54(11)*: 2856-2860 (1994)).

Reconsideration of the objection and rejections is hereby requested.

Discussion of the Objection to the Claim

The Office objects to the claim 1 for reciting "...a second poxvirus vector containing *a* one or more DNA segments..." The superfluous "a" has been removed from claim. In view of Applicants' amendment to claim 1, Applicants request that the objection to claim 1 be withdrawn.

Discussion of the Indefiniteness Rejection

The Office contends that the recitation of "or modified version thereof" is indefinite because the gene can be modified to the extent of becoming a totally random sequence. Applicants have amended claim 1 to recite a wobbled version of mucin, as recited in claim 13 (now canceled).

Applicants believe that the claims, as amended, are sufficiently clear. Therefore, Applicants request that the indefiniteness rejection be withdrawn.

Discussion of Obviousness Rejection

In response to Applicants' arguments, the Office maintains that the subject matter of the pending claims is obvious in view of the Laidlaw, Pecher, and Kotera references. The obviousness rejection is traversed for the following reasons.

The present invention, as defined by the pending claims, is directed to a method for inducing an immunological response against a malignant pancreatic cell in an individual, wherein the method comprises (a) selecting an individual having malignant pancreatic cells or at risk for developing such a pancreatic tumor, (b) administering to the individual a first poxvirus vector containing one or more DNA segments that encode (i) CEA or an antigen portion thereof and (ii) MUC or an antigen portion thereof or a wobbled version thereof, and (c) at regular intervals thereafter administering at least a second poxvirus vector containing one or more DNA segments that encode (i) CEA or an antigen portion thereof and (ii) MUC or an antigenic portion thereof or a wobbled version thereof, such that an immunological response against the malignant pancreatic cell is induced in the individual.

The Office contends that the Laidlaw reference discloses a poxvirus vector, which can express CEA or MUC-1, which are established tumor associated antigens (TAAs) for colon and breast cancers. The Office contends that the Laidlaw reference teaches that immunization of mice using a heterologous prime/boost protocol with two different vectors encoding multiple antigens (i.e., the MEI polypeptide which comprises epitopes from a viral antigen and murine tumor antigens) resulted in an improved immune response over homologous immunization with either vector alone. The Office acknowledges that the Laidlaw reference does not disclose a first and a second vector containing a DNA segment

encoding CEA and MUC, or the administration of the vectors to produce an immunological response against a malignant pancreatic cell. However, the Office contends that the Pecher reference discloses a pharmaceutical composition for treating and preventing human tumors, which express CEA and/or MUC-1, and the use thereof as a vaccine for activating the immune system. The Office relies on the Kotera reference for its disclosure of a tandem repeat epitope of human MUC-1 in sera from pancreatic cancer patients.

Applicants note that the Laidlaw reference does not disclose that CEA or MUC are pancreatic tumor antigens, or the administration of a first and second vector each containing a DNA segment encoding CEA and MUC to produce an immunological response against a malignant pancreatic cell, as required by the pending claims.

The deficiencies of the Laidlaw reference are not remedied by the Pecher or Kotera references.

The Pecher reference indicates that CEA and/or MUC-1 are expressed by human tumors and *not* by one vector, as required by the pending claims. Specifically, the Pecher reference discloses a pharmaceutical composition comprising one vector (e.g., a plasmid) comprising the gene encoding MUC-1 and/or another vector (e.g., a plasmid) comprising the gene encoding CEA. Thus, CEA and MUC-1 are not in the same vector as required by the pending claims. Additionally, the Pecher reference does not identify CEA and/or MUC-1 as pancreatic tumor antigens, or disclose the administration of a first and a second vector containing a DNA segment encoding CEA and MUC-1 to produce an immunological response against a malignant pancreatic cell, as required by the pending claims.

While the Kotera reference identifies a tandem repeat epitope of human MUC-1 in sera from pancreatic cancer patients, the Kotera reference does not disclose a vector encoding MUC-1, much less a first and second vector containing a DNA segment encoding CEA and MUC-1, or the administration of the vectors to produce an immunological response against a malignant pancreatic cell, as required by the pending claims. Furthermore, the Kotera reference does not disclose that CEA is a pancreatic tumor antigen.

Thus, none of the cited references, when considered alone or in combination, teach or suggest inducing an immunological response against a malignant pancreatic cell by

administering a first poxvirus vector containing one or more DNA segments that encode (i) CEA or an antigen portion thereof and (ii) MUC or an antigen portion thereof or a wobbled version thereof, and (c) at regular intervals thereafter administering at least a second poxvirus vector containing one or more DNA segments that encode (i) CEA or an antigen portion thereof and (ii) MUC or an antigenic portion thereof or a wobbled version thereof, as required by the claims.

As discussed in the previous Reply to Office Action, the inventive methods result in unexpected benefits, which further evidence the nonobviousness of the present invention, as defined by the pending claims, over the combination of the disclosures of the cited references. In particular, the inventive methods result in the beneficial effect of stimulating the immune system to target against the CEA and MUC-1 antigens, which are found on over 90% of pancreatic tumor cells (see, e.g., Example 11 of the specification). As a result, metastatic pancreatic cancer patients receiving this vaccine were shown to have a trend toward an overall survival greater than the expected median overall survival (see Abstract of Schuetz et al., *J. Clin. Oncol., 2005 ASCO Annual Meeting Proceedings, 23(16S Part I of II in June 1 Supplement)*: 2576 (2005); submitted herewith).

The benefits attendant the present invention are unexpected and surprising in view of the teachings in the art at the earliest priority date of the application. As evidenced by Palmowski et al. (*J. Immunol., 168*: 4391-4398 (2002); submitted herewith) and Brody et al. (*Immunol., 22*: 75-85 (1972); submitted herewith), prior to the invention, the presentation of two antigens together (at the same location) was thought to to result in competition between the two antigens with one antigen being dominant, thereby resulting in a *reduced* immune response to one or both of the antigens (see, e.g., page 4397, second column, fourth full paragraph, of Palmoski et al., and page 83, lines 1-3, of Brody et al.).

For these reasons, the subject matter of the pending clams would not have been obvious to one of ordinary skill in the art at the relevant time in view of the combined disclosures of the Laidlaw, Pecher, and Kotera references. Accordingly, the obviousness rejection should be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,

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